



OBLON ET AL (703) 413-3000
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INV. Jacques THEZE ET AL.
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Reply to NOTICE REGARDING DRAWINGS
DATED 06/28/2004
REPLACEMENT DRAWINGS

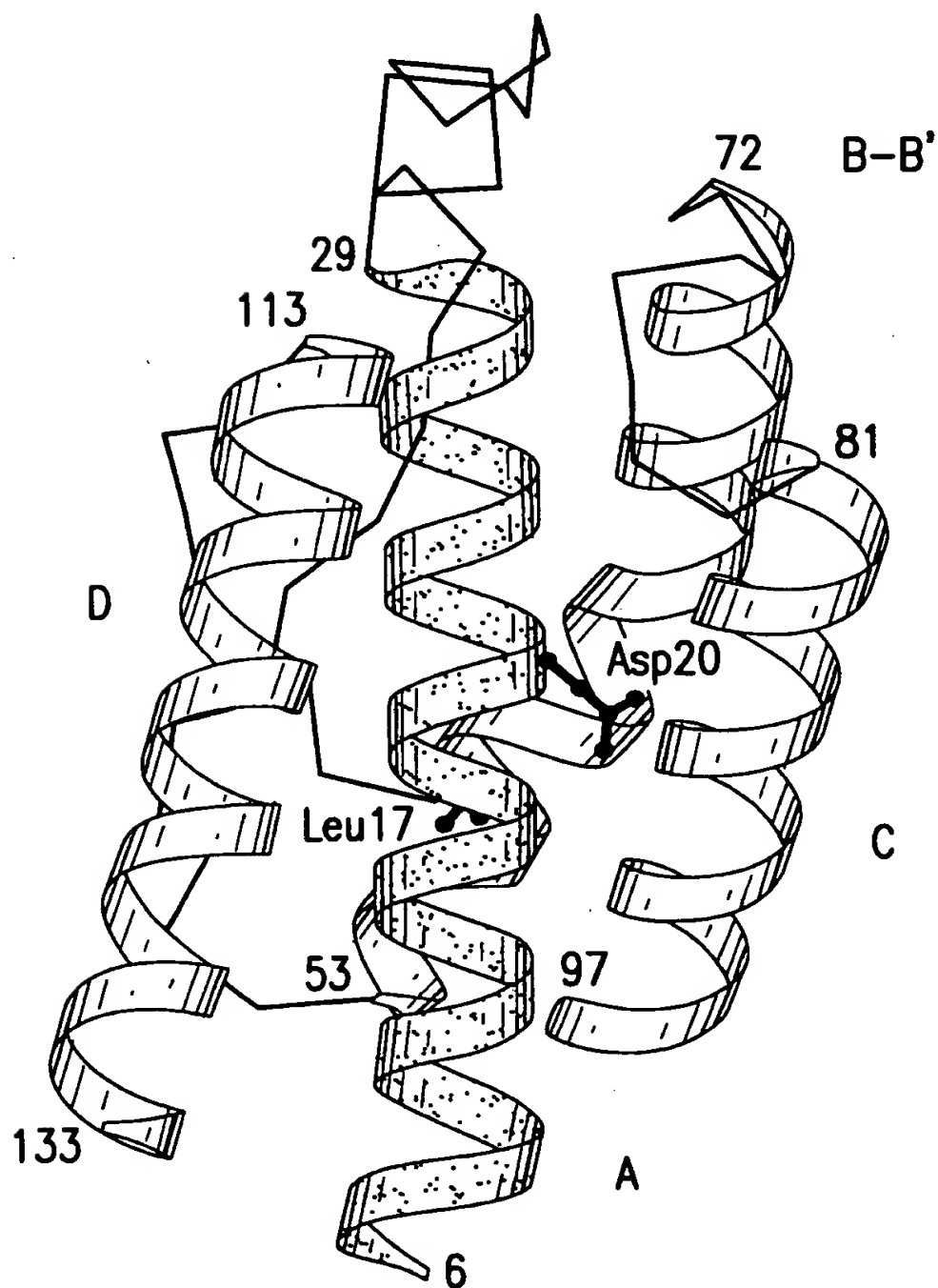


FIG. 1

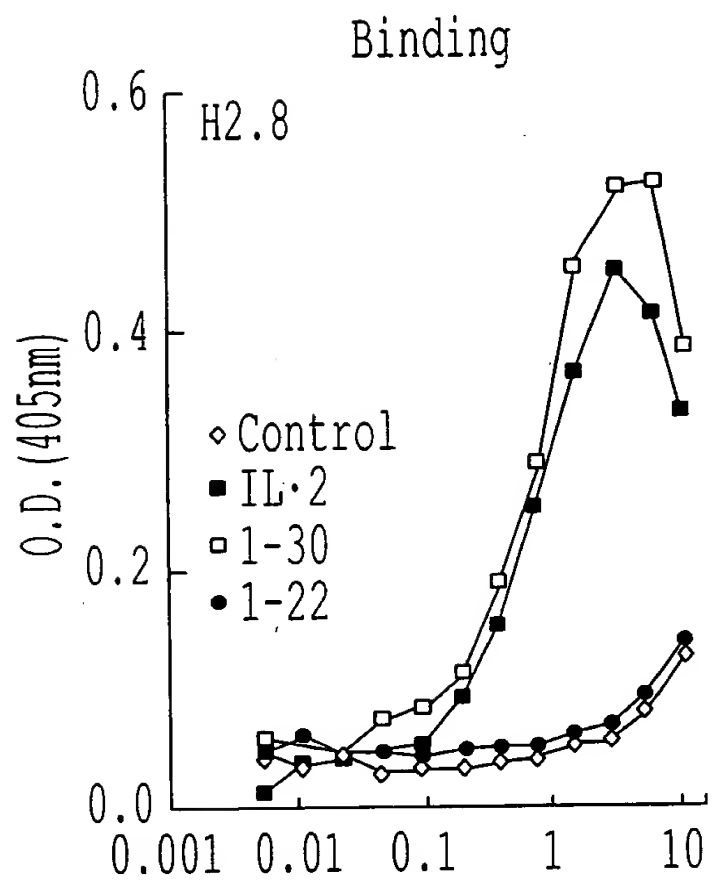


FIG. 2

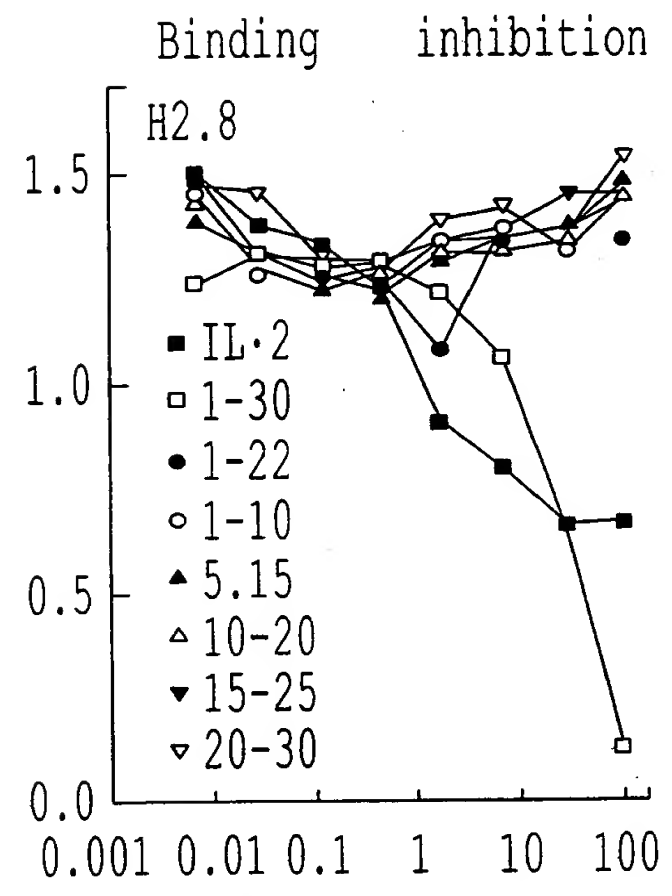


FIG. 2

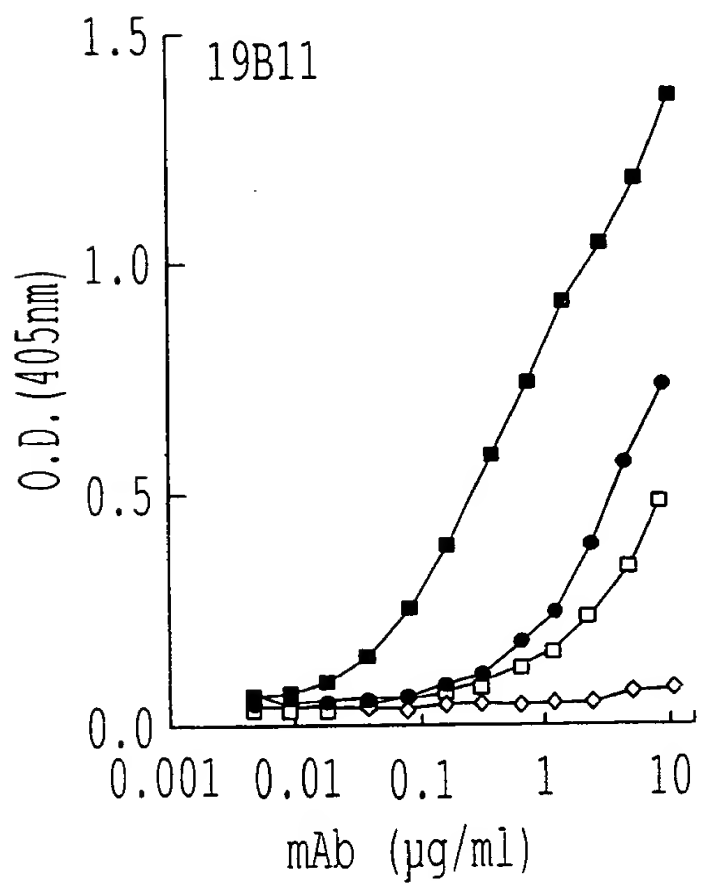


FIG. 2

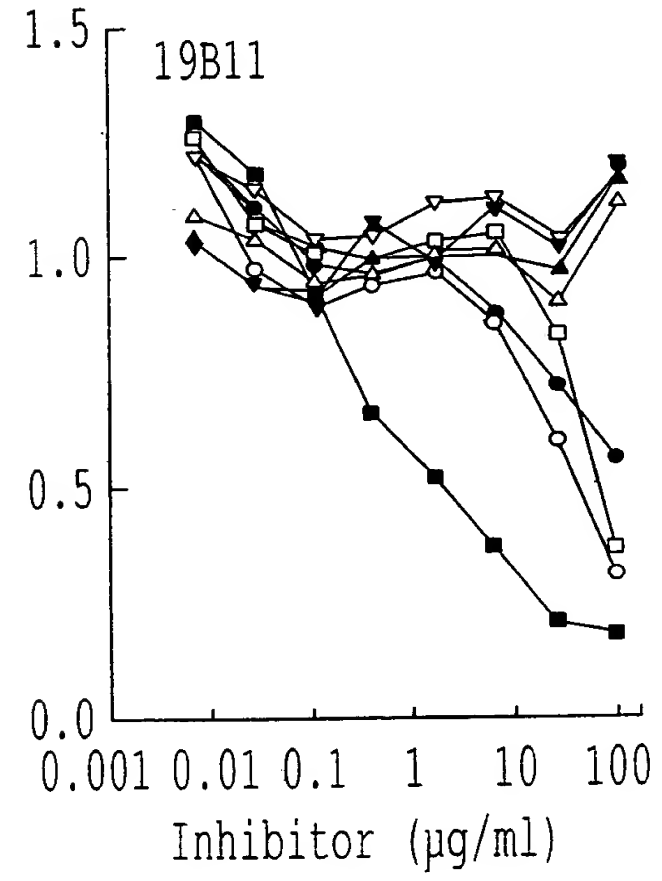


FIG. 2

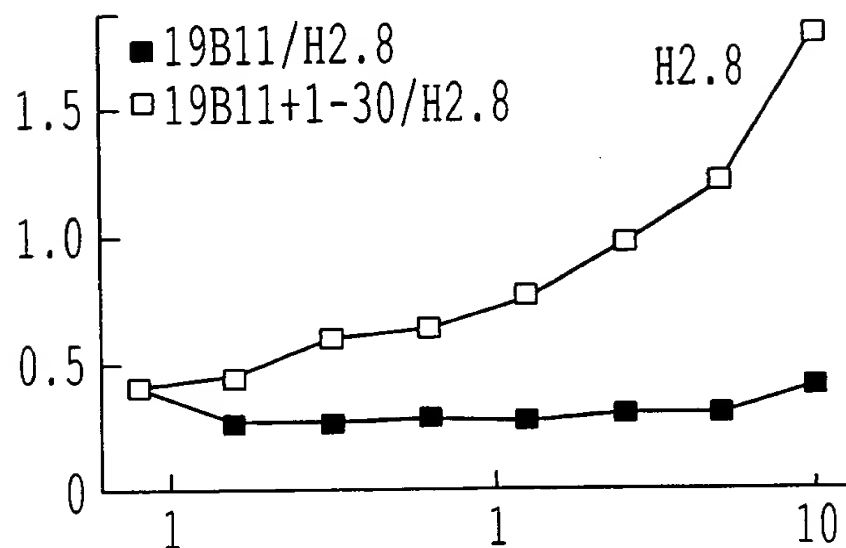


FIG. 3

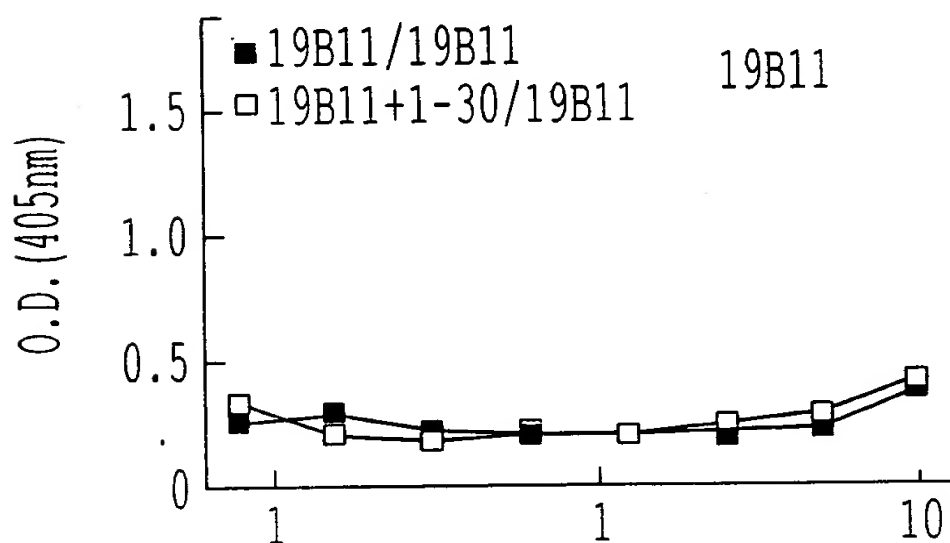


FIG. 3

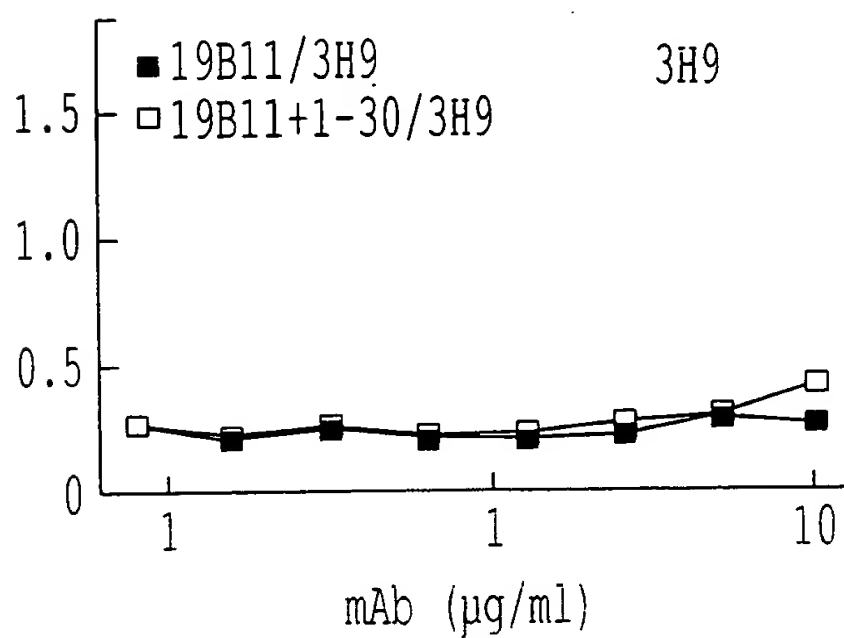


FIG. 3

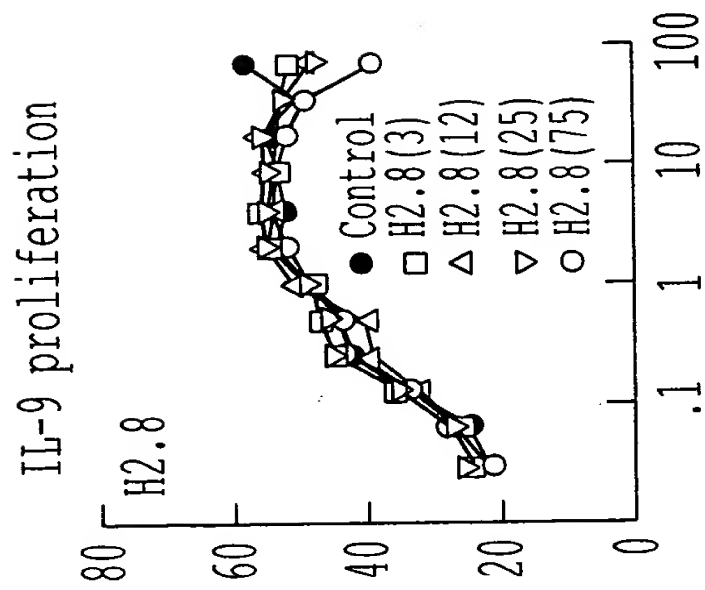


FIG. 4

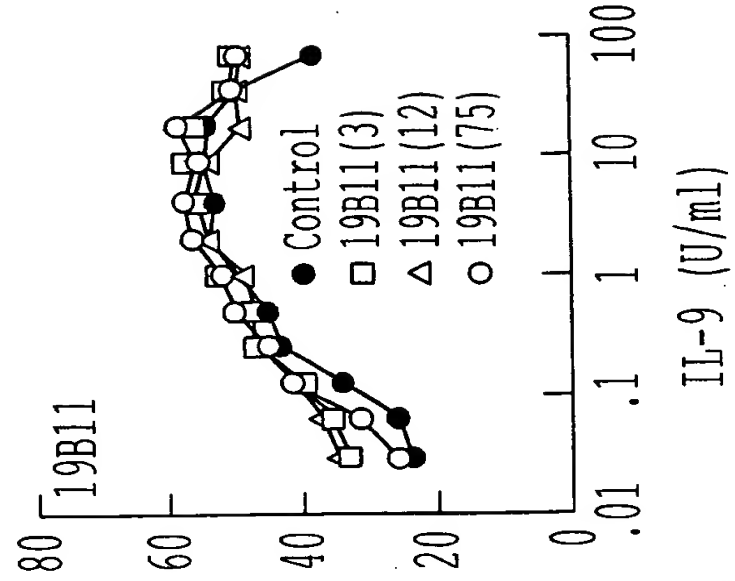


FIG. 4

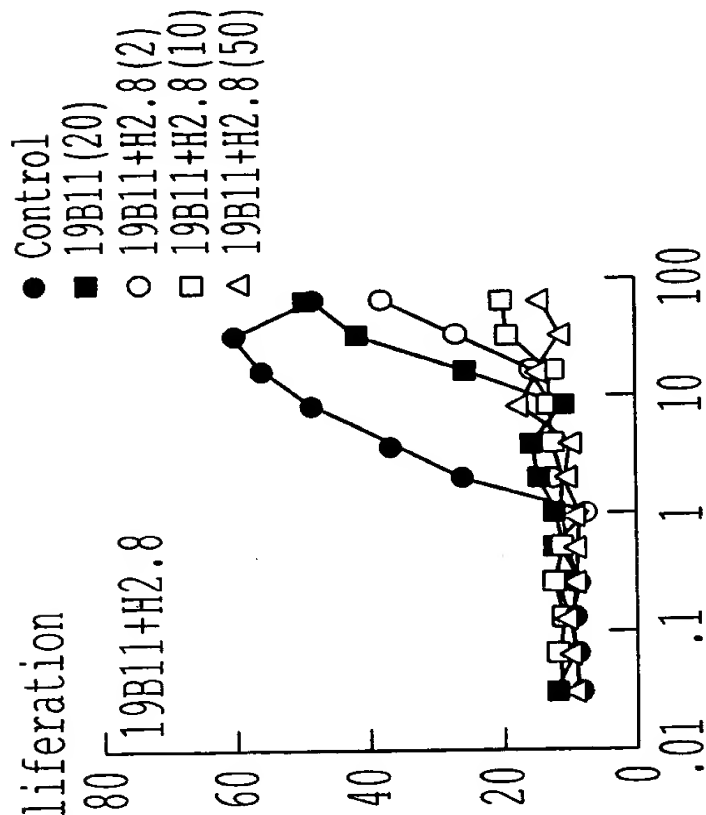


FIG. 4

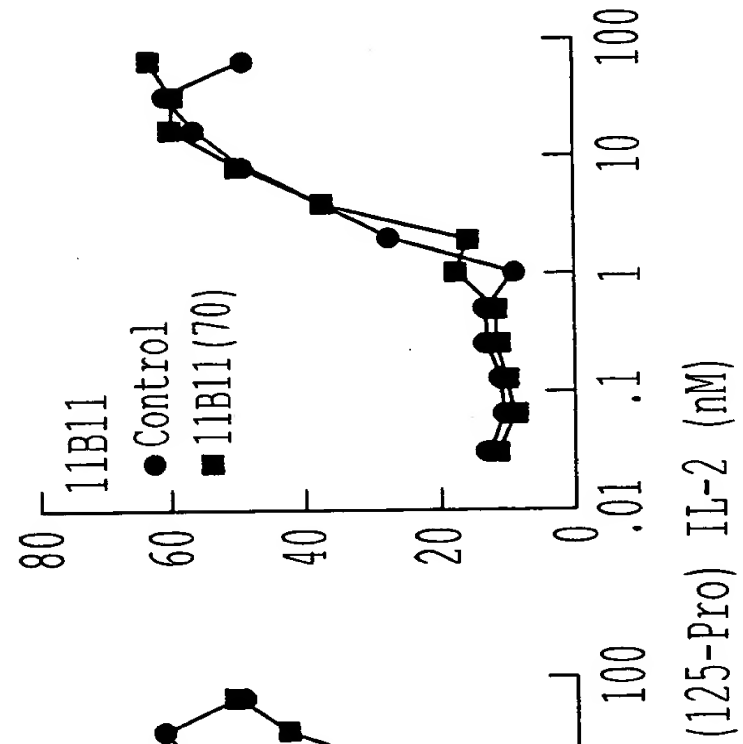


FIG. 4

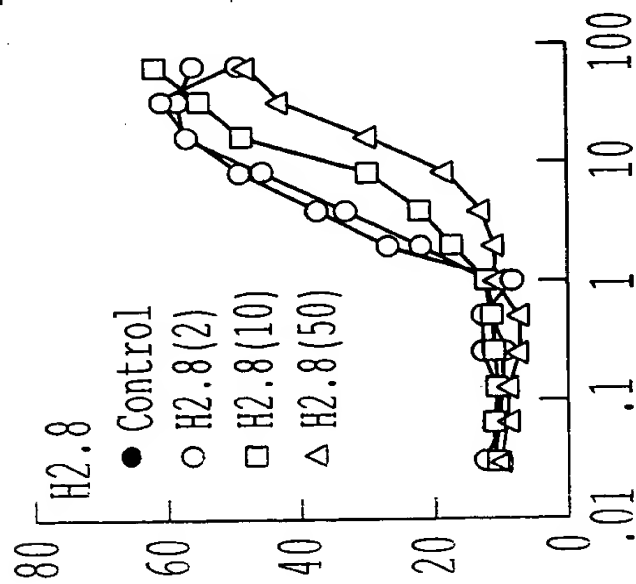


FIG. 4

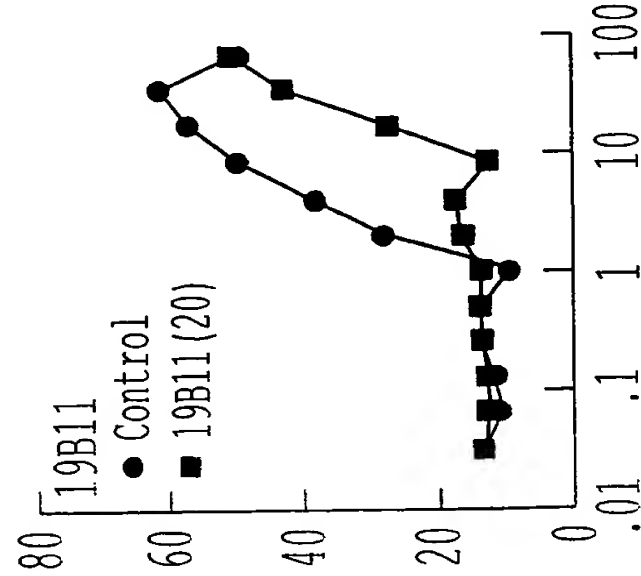


FIG. 4

[³H]TdR incorporation (x10⁻³)

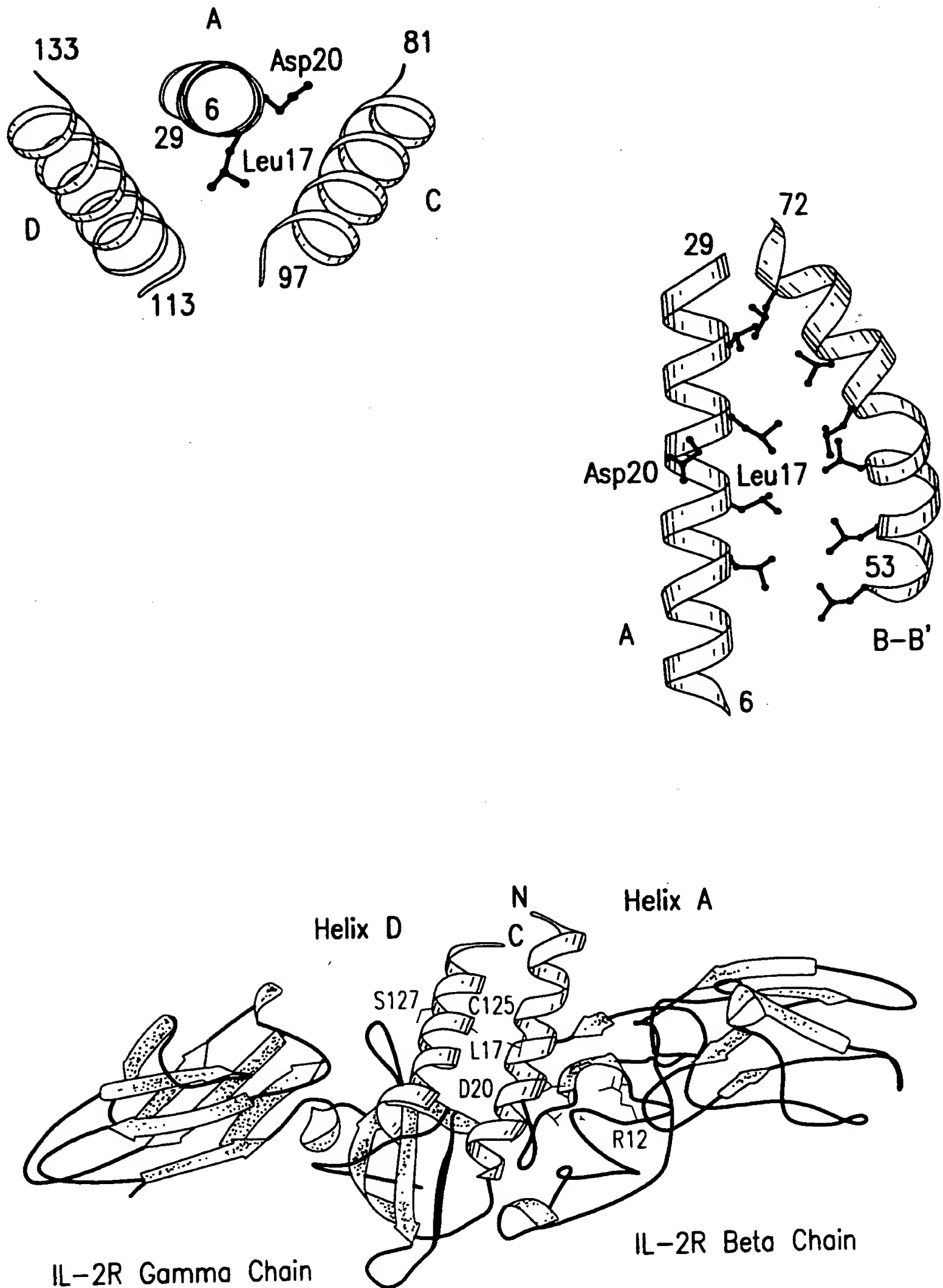


FIG.5

Interleukine-2 receptor

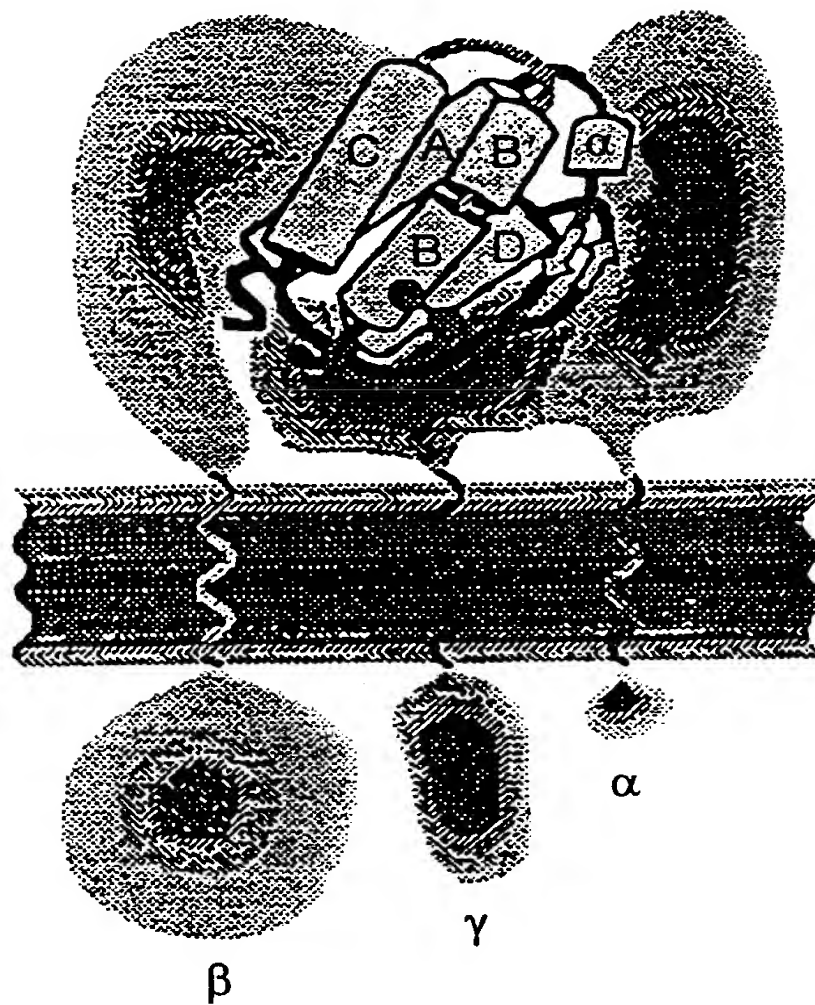


FIG.6

IL-2 AND IP130 SEQUENCE (α -HELICES ARE BOXED)

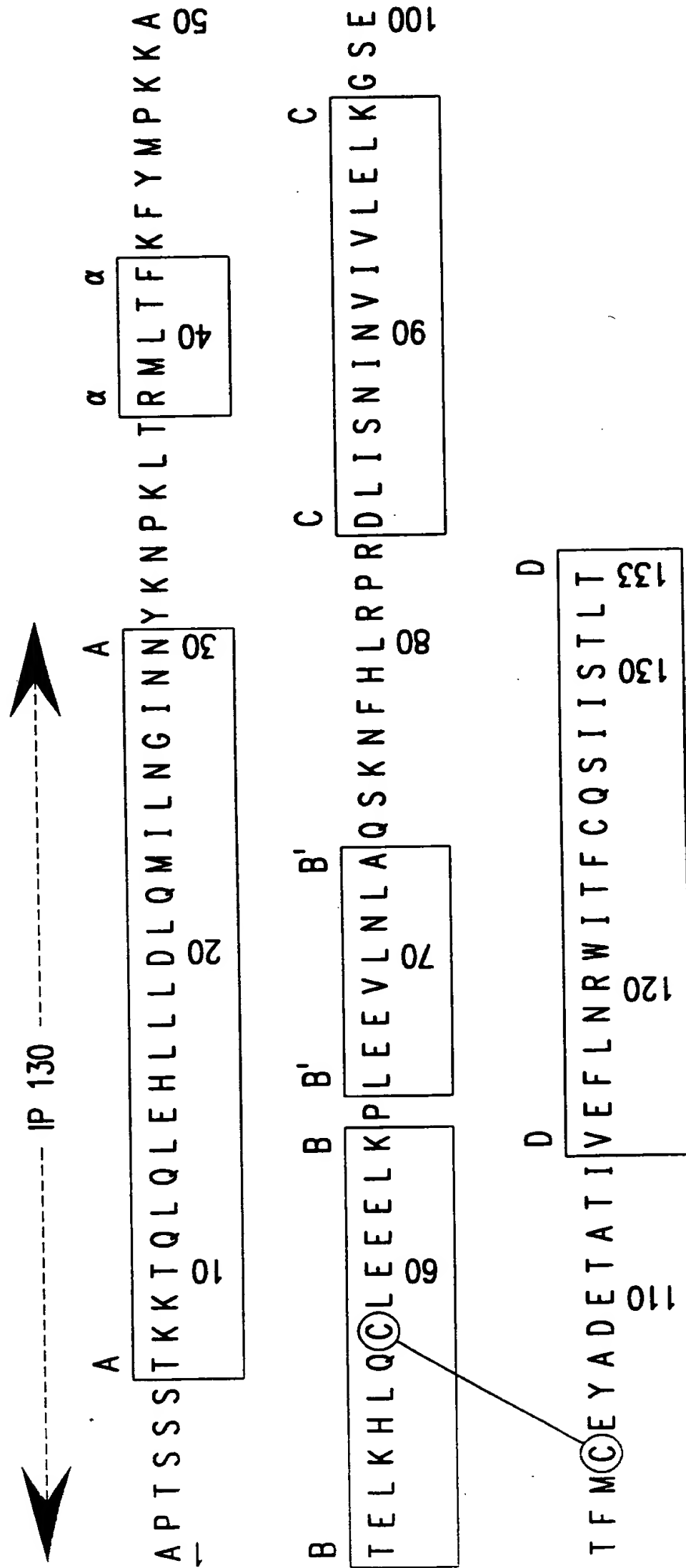


FIG.6

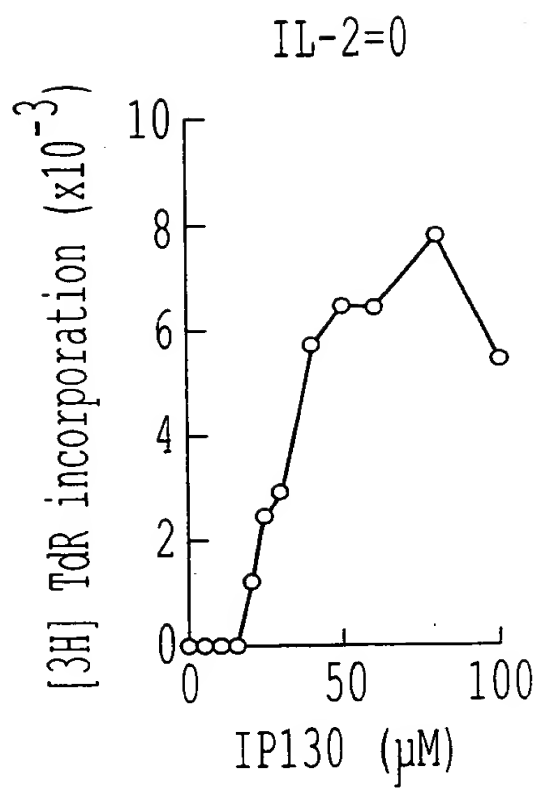


FIG. 7

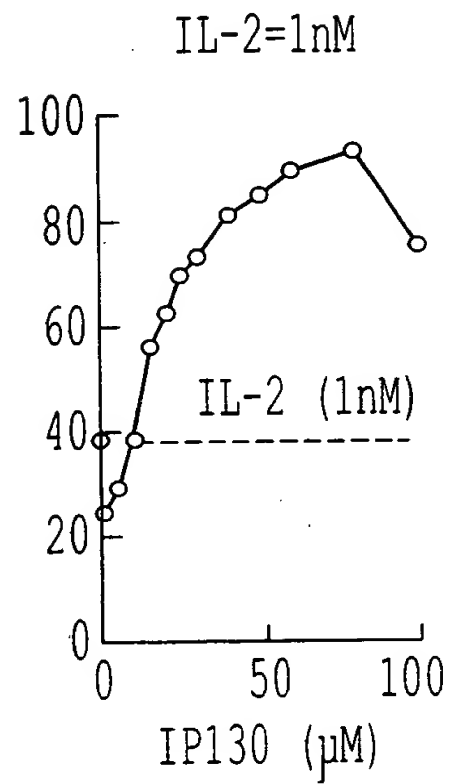


FIG. 7

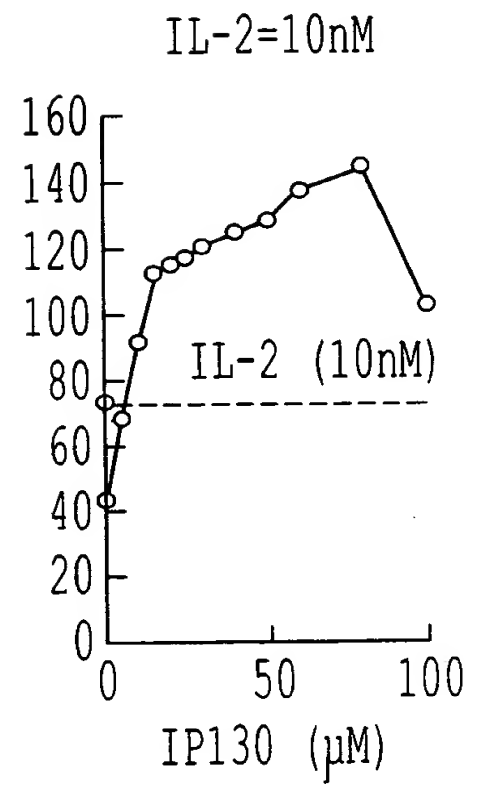


FIG. 7

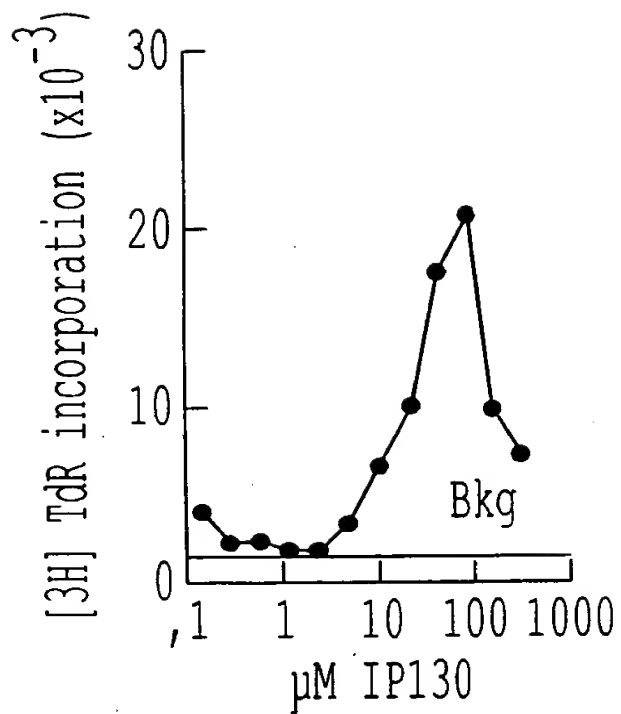


FIG. 8A

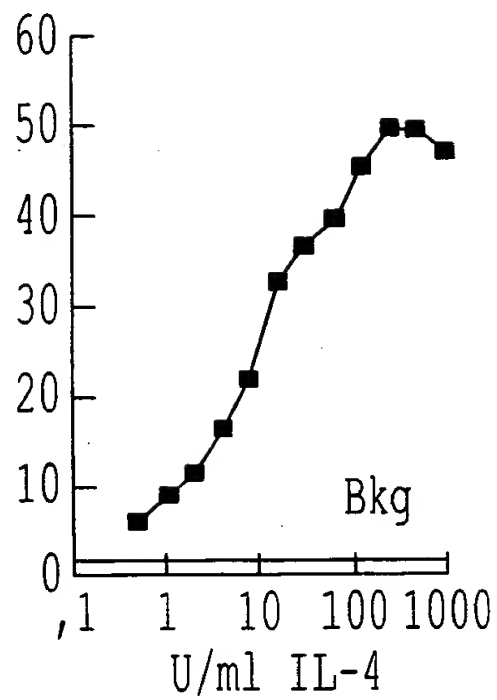


FIG. 8B

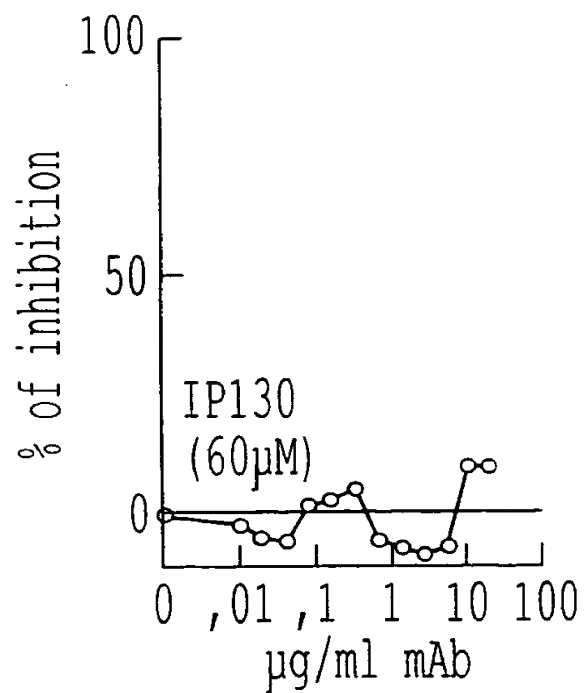


FIG. 8C

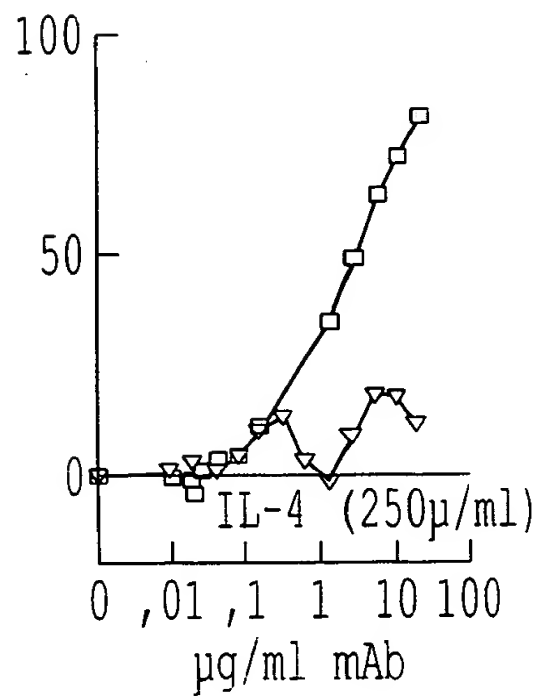


FIG. 8C

● IL-4
○ IL-4 IP130

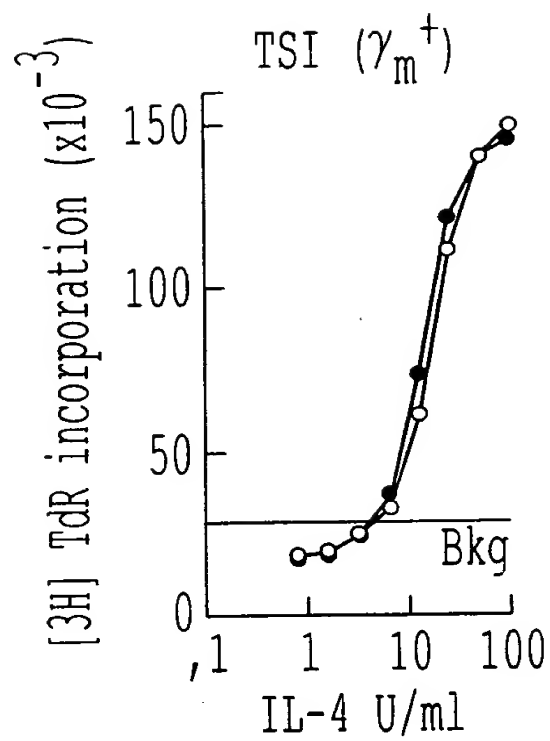


FIG. 9A

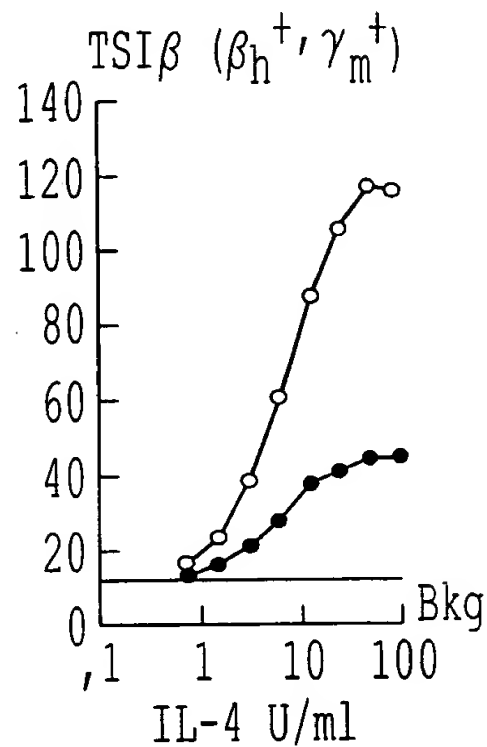


FIG. 9A

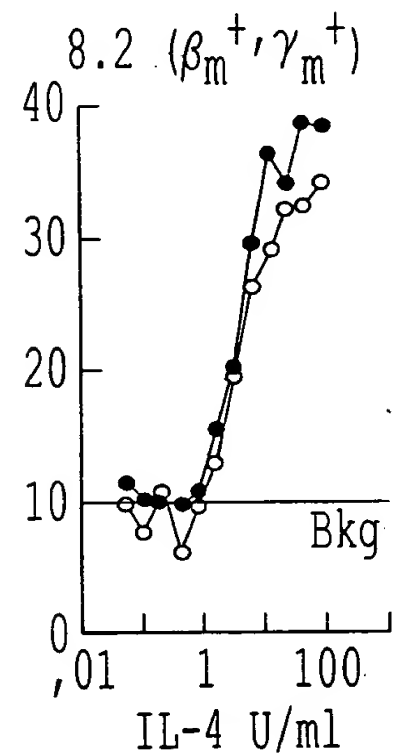


FIG. 9A

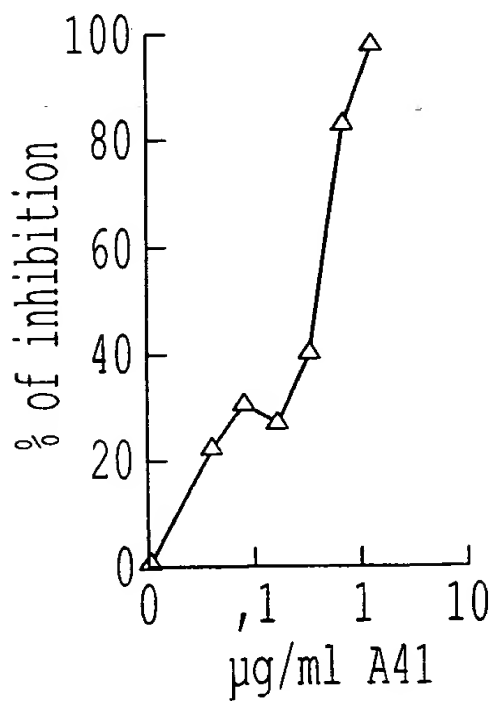


FIG. 9B

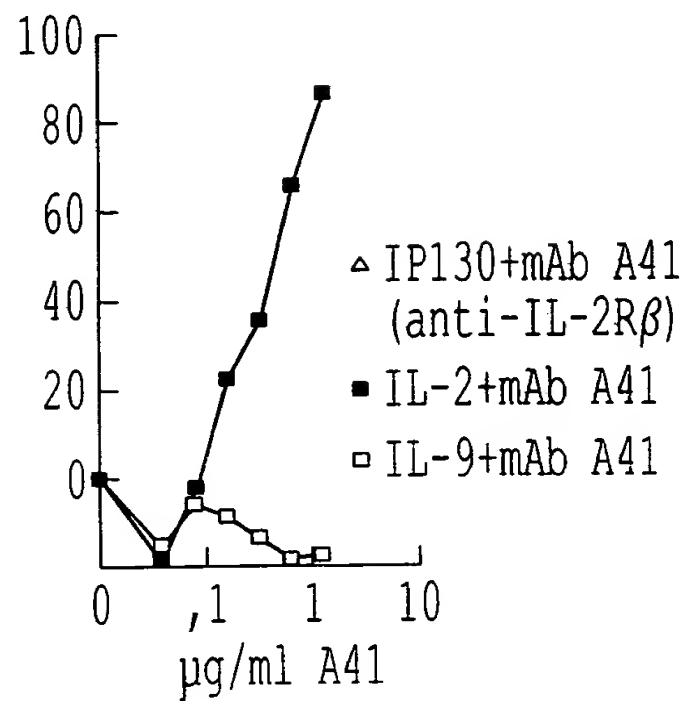


FIG. 9B

1 10 20 30
APTSSSTKKIQLEHLLDLQMILNGINN

% helix
(Circular dichroism)

Main molecular species

Activity

1 30

Tetramer (4M-8M, Kd=30-100μM)
/Octamer

+++
++

10 30

Dimer (1M-2M, Kd=0,2μM)
/Telramer (2M-4M, Kd=100μM)

-

1 22

<2%

-

1 10

Dimer (1M-2M, Kd=50μM)
(2M-4M, Kd=1,4mM)

-

5 15

Dimer (1M-2m, Kd=113μM)

-

10 20

Monomer

ND

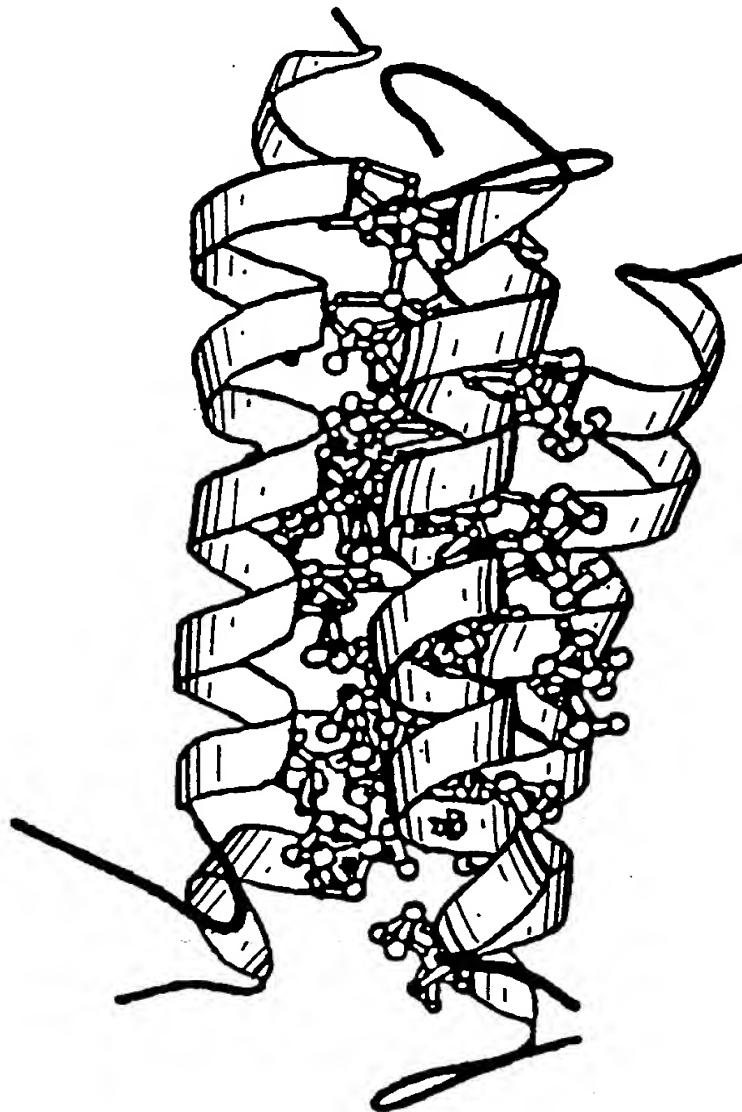
20 30

Monomer

+

<5%

FIG. 10



IP130

FIG.11

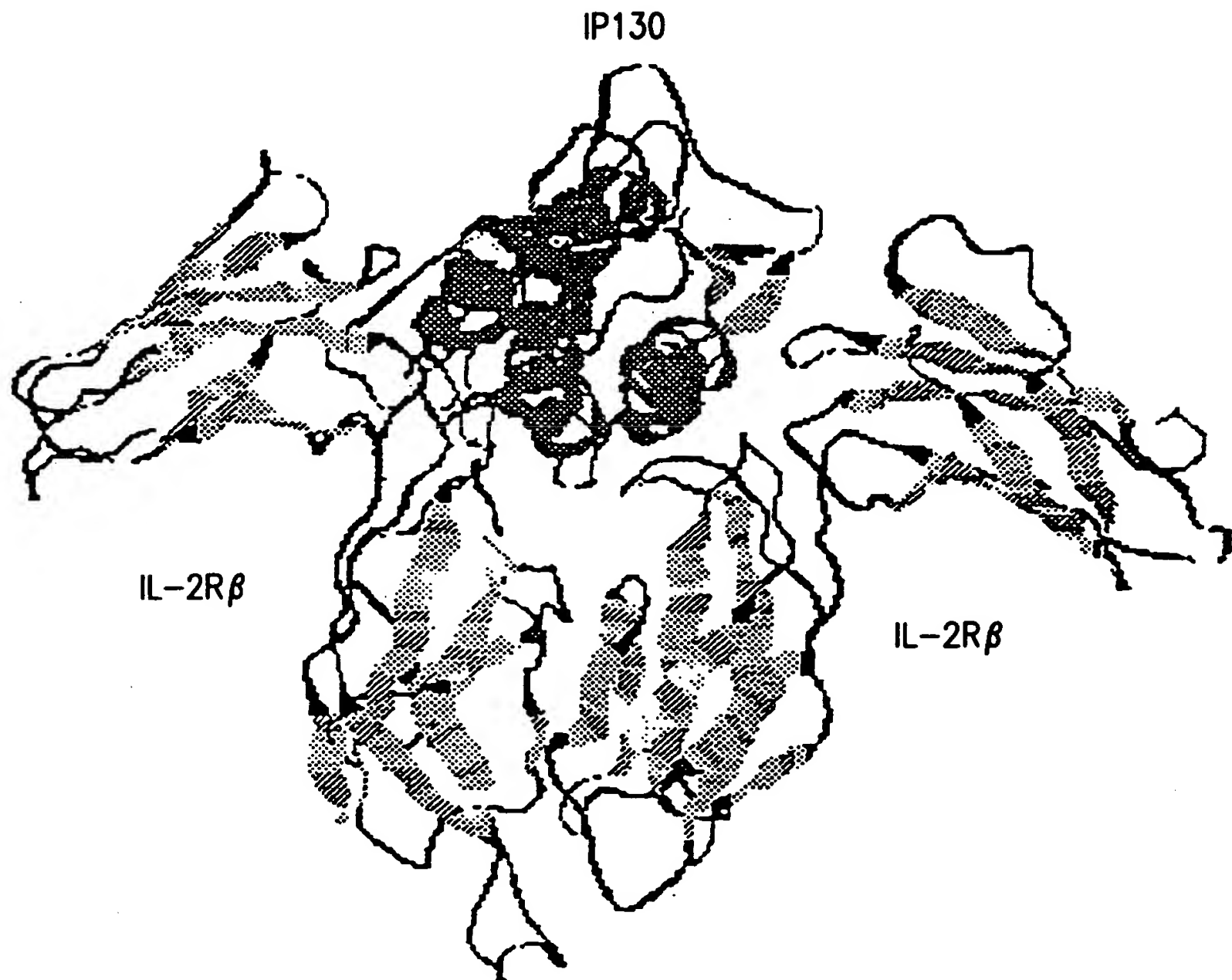
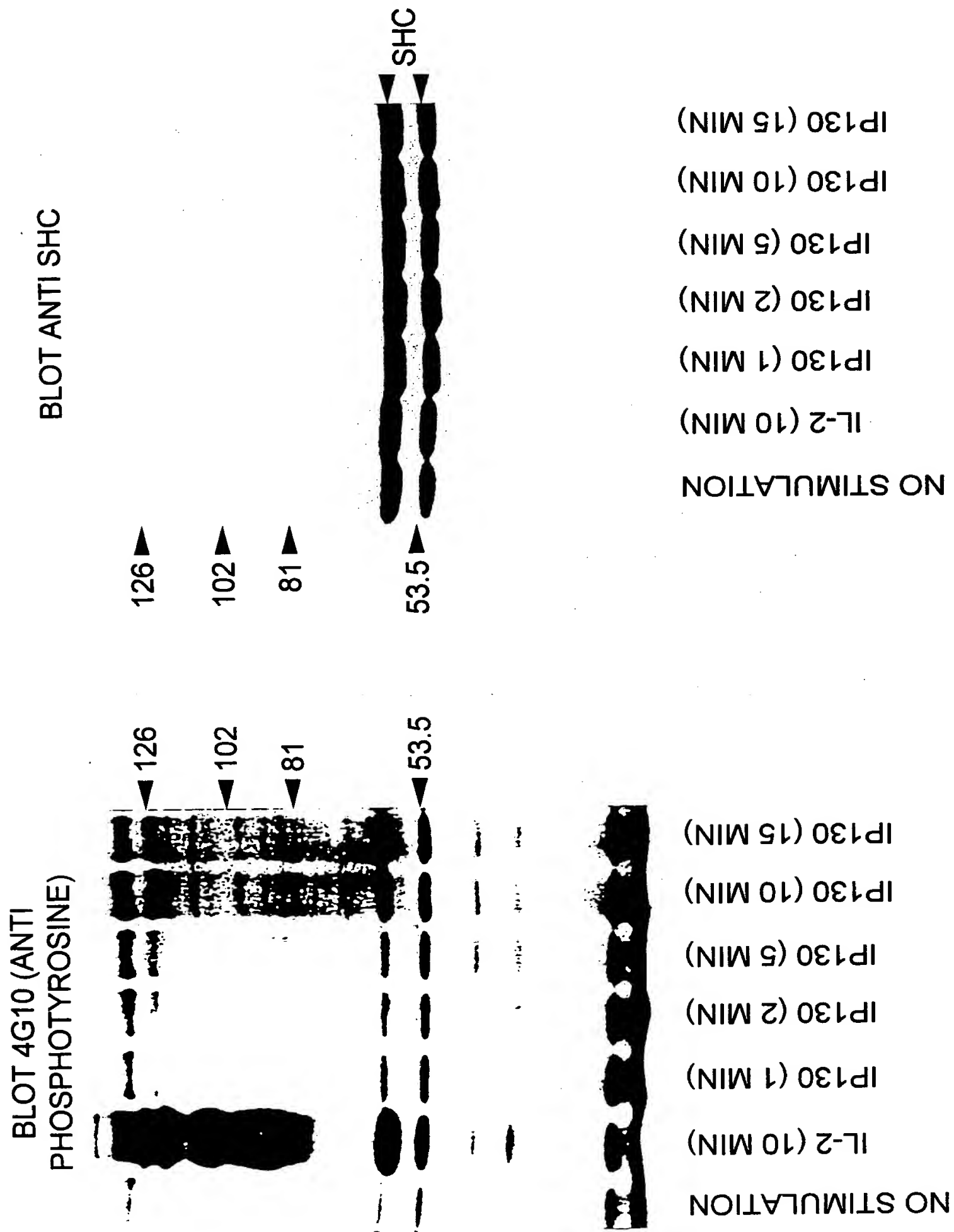


FIG.11



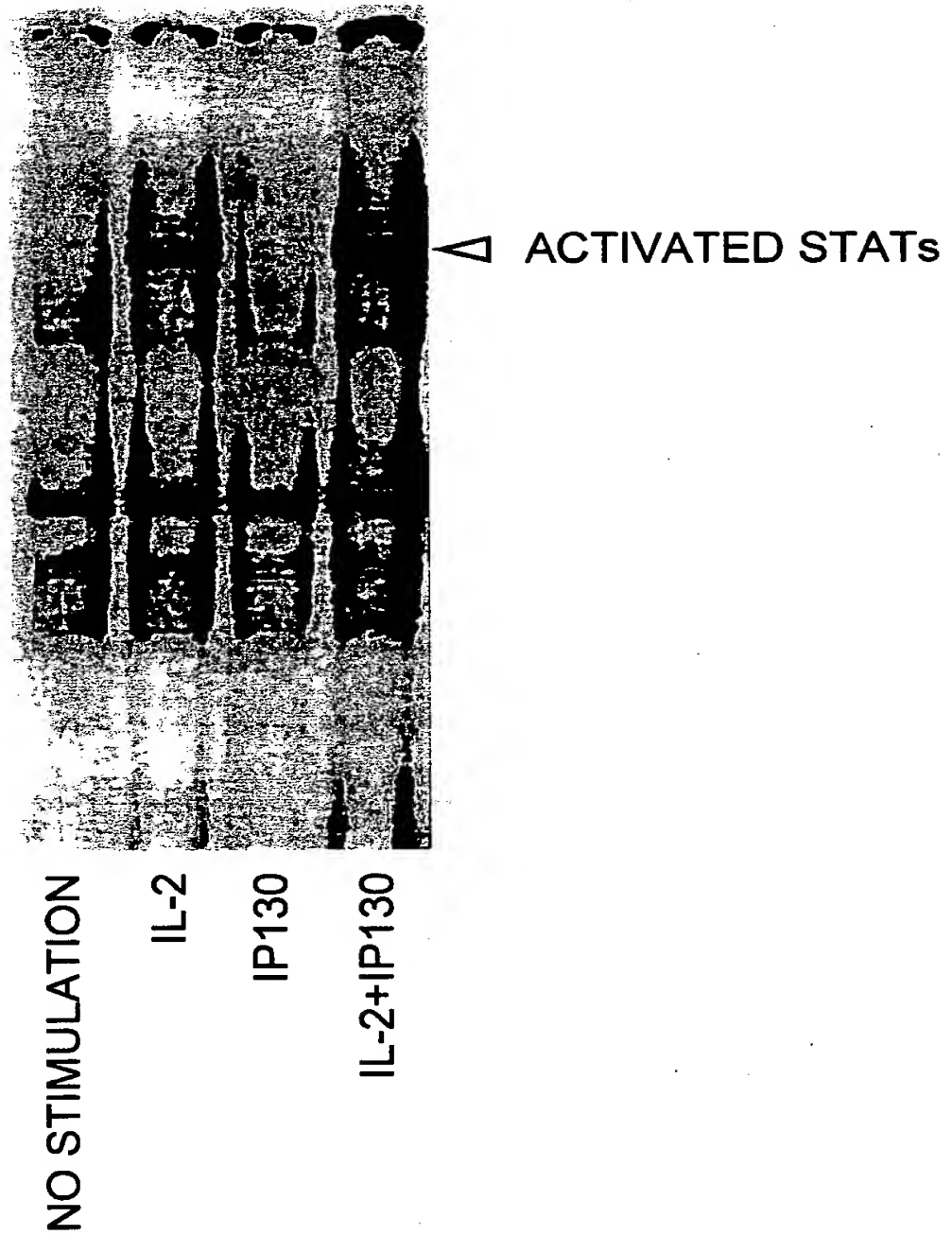
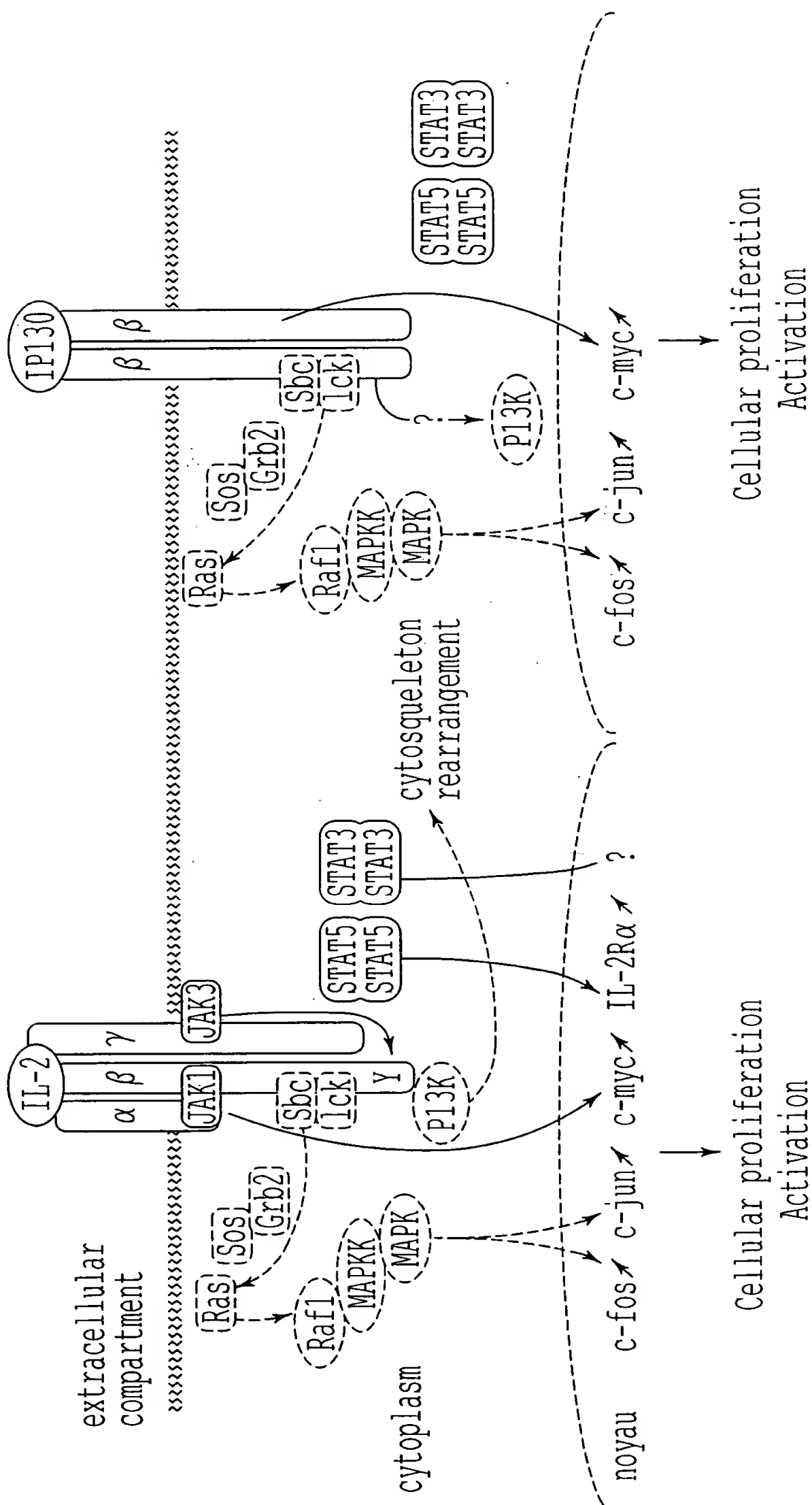


FIG. 13



IL-2 receptor and its major signal transduction pathway Model of transduction pathway induced by IP130

FIG. 14

NK cells (CD56⁺) entering in S+G2/M phases after IP130 stimulation
(synergy with IL-2)

Treatment		J31	J32	J33
IL-2 50 nM		14	12	14
	IP130 60 μ M	0	17	≤ 5
	IP130 120 μ M	0	14	< 5
IL-2 50 nM +	IP130 60 μ M	26	21	7
IL-2 50 nM +	IP130 120 μ M	28	28	28

FIG. 15

Stimulation
3 Days

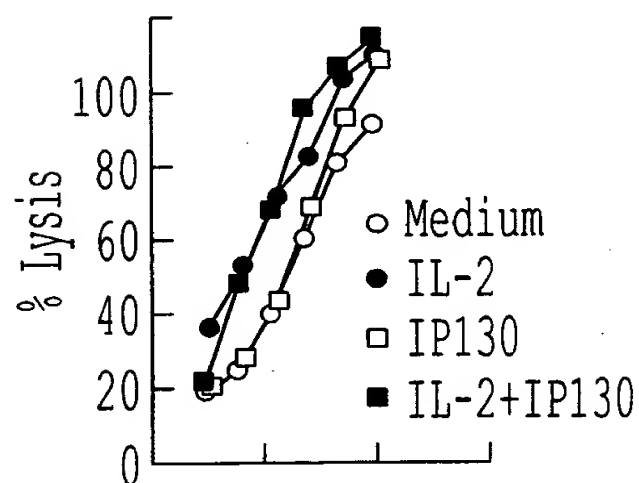


FIG. 16

Effector / target=10

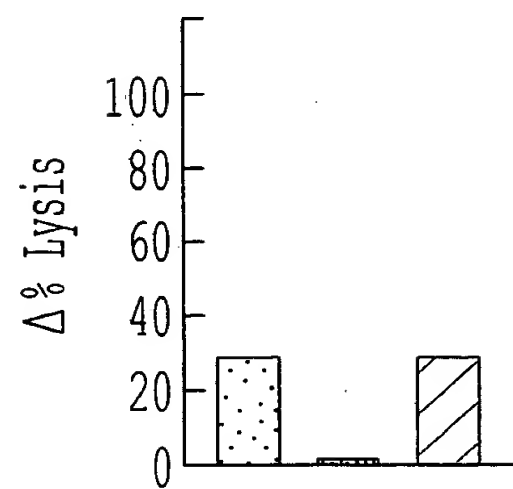


FIG. 16

6 Days

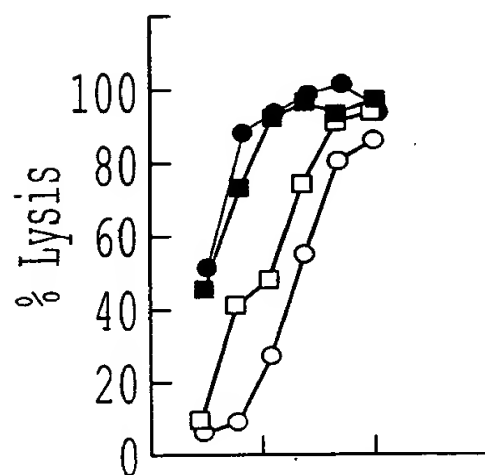


FIG. 16

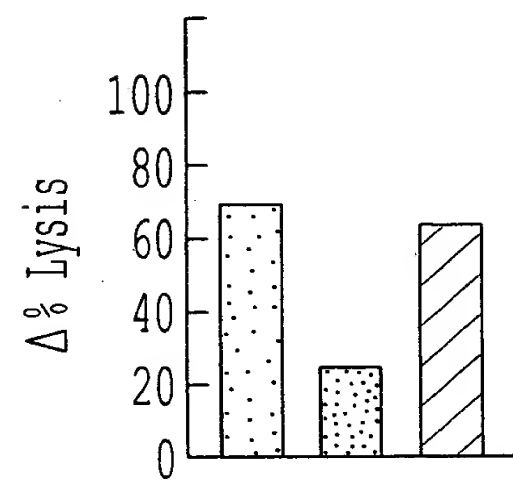


FIG. 16

9 Days

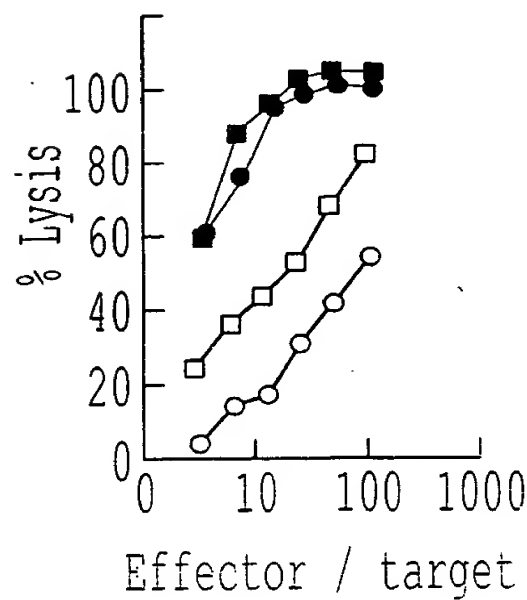


FIG. 16

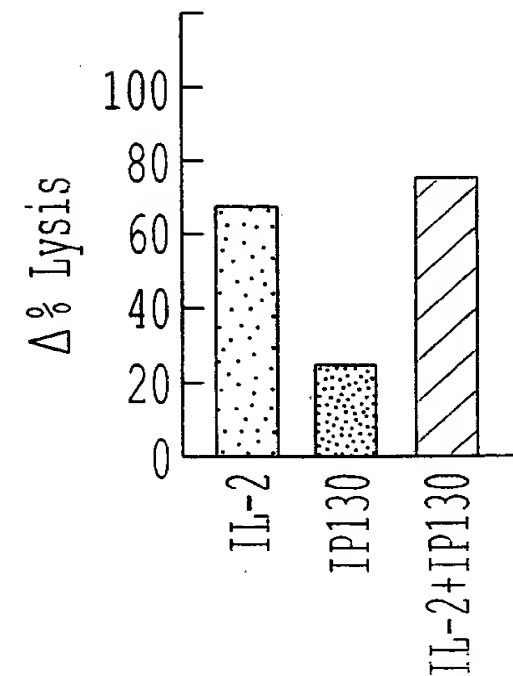


FIG. 16